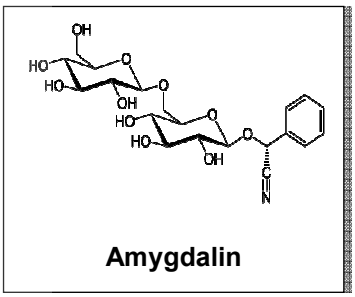
UNIT 19

AROMATIC ALDEHYDES AND KETONS

Structure

19.1 INTRODUCTION

In the previous unit, we have already discussed the chemistry of aliphatic aldehydes and ketones. Aromatic aldehydes and ketones also show the usual reactions associated with carbonyl group but they display some unique reactions arising from the influence of the aromatic group. Benzaldehyde and phenylethanone (acetophenone) are the simplest example of aromatic aldehydes and ketones, respectively. Benzaldehyde is present in bitter almonds in the form of its glucoside, **amygdalin** ($C_{20}H_{27}O_{11}N$). When amygdalin is boiled with dilute acids, it hydrolyses and converts into benzaldehyde, HCN and glucose. Phenylethanone, which is known by its preferred name acetophenone, is naturally found in several fruits. It has distinct organic scent. Thus, it is often used in scenting lotions and flavoring foods. Acetophenone has also been used in medicine as hypnotic under the trade name hypnone. In this unit, we will take up preparations and reactions of benzaldehyde and acetophenone in detail.



Amygdalin

Expected Learning Outcomes

After studying this unit, you should be able to:

- explain how aromatic aldehydes and ketones can be prepared; and
- describe the reactions due to both carbonyl group and aromatic ring of aromatic aldehydes and ketones.

19.2 PREPARATION OF BEZALDEHYDE AND ACETOPHENONE

Benzaldehyde can be obtained by the following methods.

i) By Hydrolysis of (dichloromethyl)benzene (benzal chloride)

Benzaldehyde is prepared by the hydrolysis of (dichloromethyl)benzene (benzal chloride) in either aqueous acid or aqueous alkali.

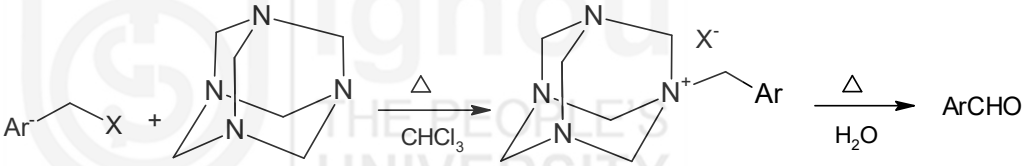
$$C_6H_5CHCl_2 + OH^- \text{ or } H_3O^+ \longrightarrow C_6H_5CHO$$

ii) By oxidation of (chloromethyl)benzene

Mild oxidising agents like copper or lead nitrate convert (chloromethyl)benzene (benzyl chloride) into benzaldehyde while reagents like HNO_3 convert it into benzoic acid.

$$2\,C_6H_5CH_2Cl \xrightarrow{\text{aq. } PbNO_3} 2C_6H_5CHO + PbCl_2 + 2HNO_3$$

(Chloromethyl)benzene can also be converted to benzaldeyde by the **Sommelet reaction**. This reaction involves refluxing (chloromethyl)benzene in aqueous solution with hexamethylenetetramine followed by hydrolysis.



iii) Oxidation of methylbenzene (toluene)/phenylmethanol (benzyl alcohol)

Methylbenzene (toluene) can be oxidised with chromium trioxide and ethanoic anhydride (acetic anhydride) or with chromyl chloride (Etard' reaction) to gives benzaldehyde:

$$C_6H_5CH_3 \xrightarrow[\text{or } CrOCl_2]{CrO_3/(CH_3CO)_2O} C_6H_5CH(OAc)_2 \xrightarrow{H_3O^+} C_6H_5CHO$$

In this preparation, acetic anhydride prevents further oxidation of benzaldehyde by converting it into diacetate. Subsequent hydrolysis generates the aldehyde group. Phenylmethanol (benzyl alcohol) can also be oxidised to benzadehyde using chromium trioxide in acetic acid.

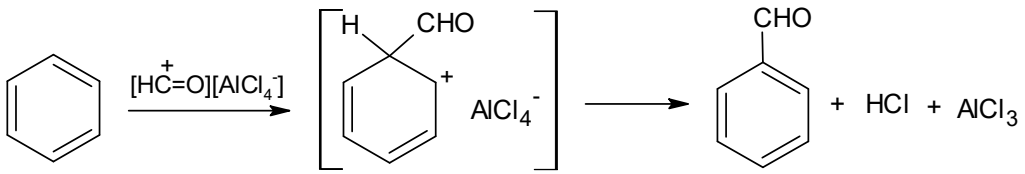
$$C_6H_5CH_2OH \xrightarrow{CrO_3,\ AcOH} C_6H_5CHO$$

iv) By direct formylation of benzene

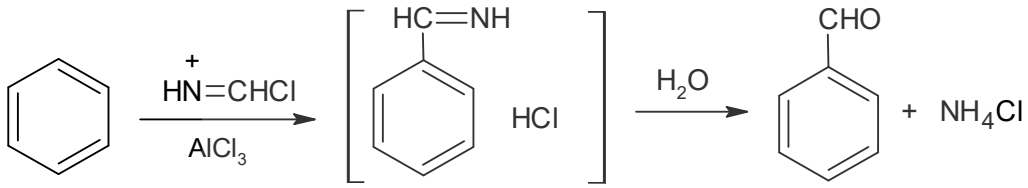
There are several methods for the introduction of the formyl group (–CHO) into aromatic ring. You have already studied Gattermann-Koch formylation and Gattermann synthesis in the previous unit. In Gattermann-Koch reaction carbon monoxide and hydrogen chloride are

passed through a solution containing benzene and aluminium chloride.

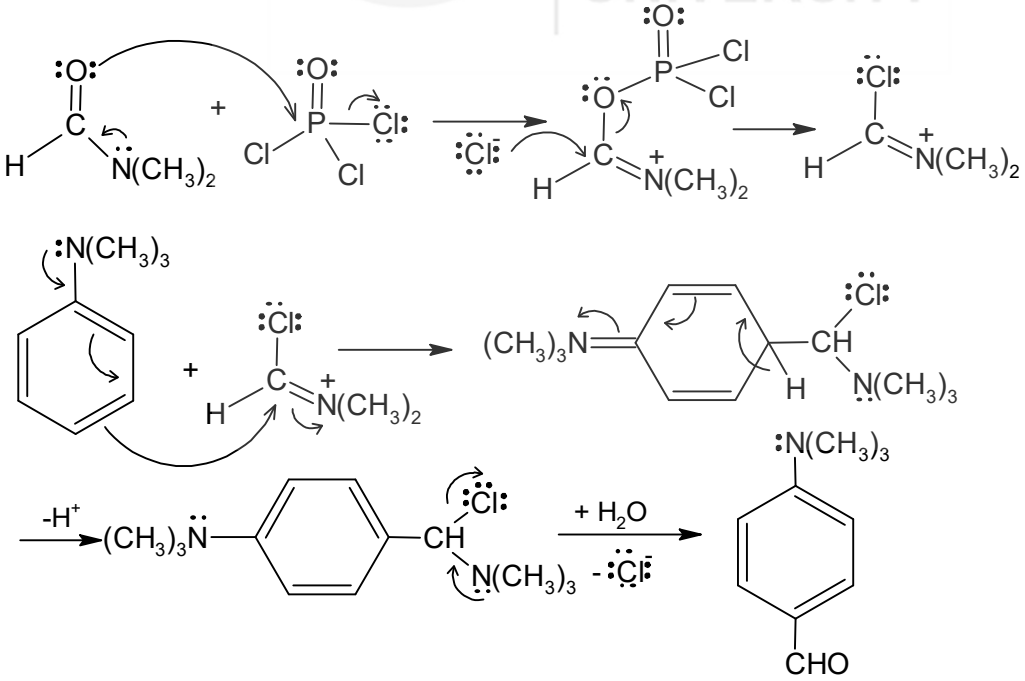
Formyl cation ($H\overset{+}{C}=O$) formed during reaction undergoes electrophilic substitution with benzene.



In a related reaction, Gattermann synthesis, the carbon monoxide is replaced by hydrogen cyanide. This reaction precedes *via* aryl imine followed by treatment with water.



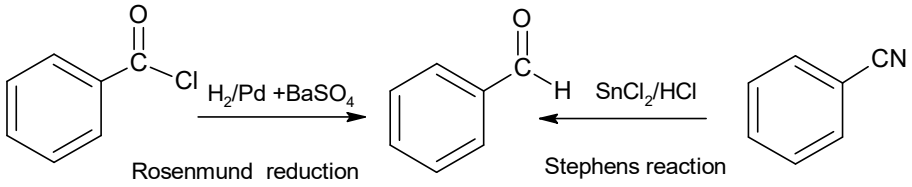
There is another interesting example of formylation reaction called Vilsmeier-Haack reaction. Activated aromatic compounds such as phenols, aryl ethers and aryl amines can be formylated by a mixture of *N,N*-dimethylformamide [$HCON(CH_3)_2$] and phosphorus oxychloride ($POCl_3$). The reaction involves electrophilic attack of a intermediate, chloroiminium ion [$(CH_3)_2N{=}CHCl$], which is formed by the reaction of *N,N*-dimethylformamide and phosphorus oxychloride. Hydrolysis of dimethyl imine gives final product.



v) By Rosenmund reduction and Stephens reaction

The Rosenmund reduction is controlled hydrogenation of acid halides in presence of a catalyst poison, $BaSO_4$ or quinoline/sulphur, which prevents over reduction to alcohols. In the Stephens reaction, a nitrile

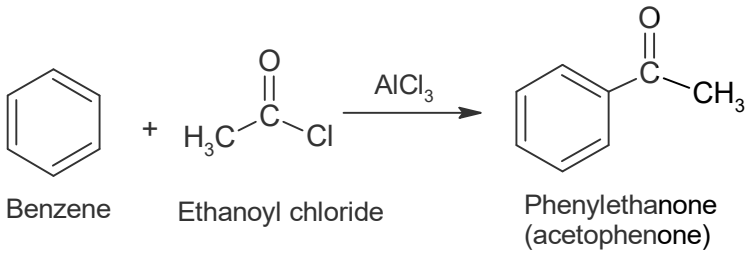
group is reduced by tin(II) chloride and HCl to imine salt which is hydrolysed to give benzaldehyde.



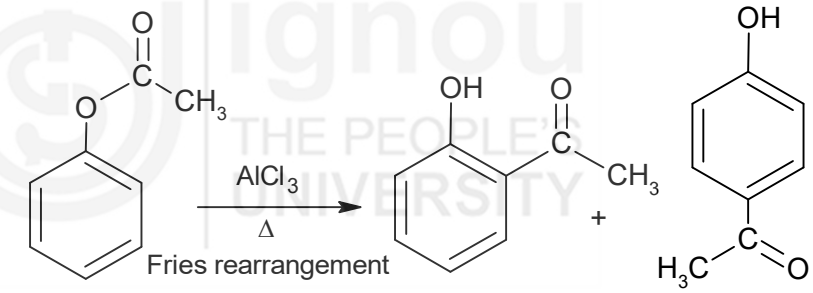
Acetophenone can be obtained by the following methods.

v) By the Friedel-Crafts Acylation Reaction

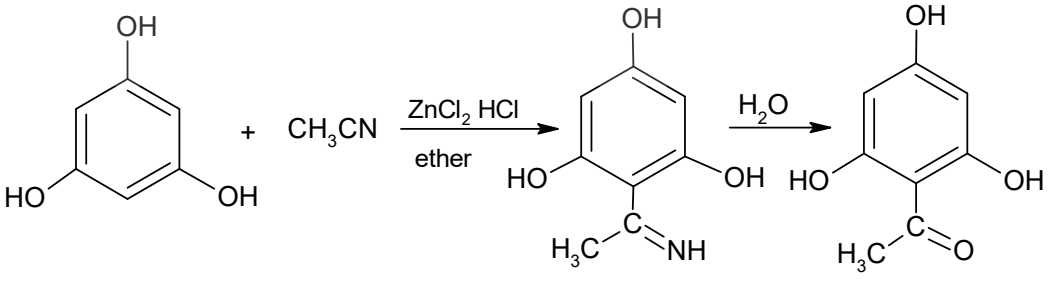
Aryl ketones can be prepared by Friedel-Crafts acylation reaction. For example, acetophenone is prepared as follows:



Phenolic aromatic ketones can be prepared by **Fries rearrangement** and **Hoesch reaction** or **Houben–Hoesch reactions**.



Hoesch reaction or Houben–Hoesch reaction is variation of Gattermann-Koch formylation. In this reaction, activated aromatic compounds such as dihydric and trihydric phenols can be acylated by reaction with acetonitrile in presence of a Lewis acid usually Zinc chloride and HCl. This reaction proceeds *via* formation of an iminium salt, which is isolated and subsequently hyrolysed.

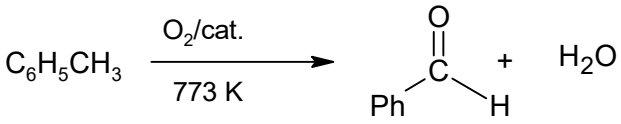


Houben-Hoesch reaction

Commercially benzaldehyde and acetophenone are preapared as follows:

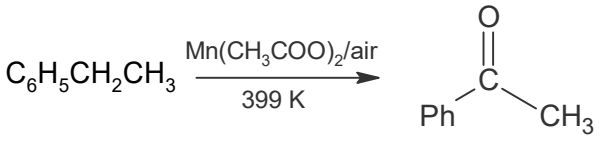
Benzaldhyde is prepared commercially by the oxidation of methylbenzene. This is done either in the vapour phase or in the liquid

phase. In the vapour phase oxidation, methylbenezene (toluene) vapours, mixed with air, are passéd over a catalyst, a mixture of oxides of manganese, molybdenum, ziroconium etc., heated to 773 K:



Liquid phase oxidation uses manganese dioxide and 65% suplhuric acid at 313 K.

Acetophenone is manufactured by the oxidation of ethylbenzene with air in the presence of manganese ethanoate as catalyst at 399 K:



SAQ 1

Benzaldehyde is obtained by the hydrolysis of:

a) methyl benzoate

b) (chloromethyl)benzene

c) (dichloromethyl)benzene

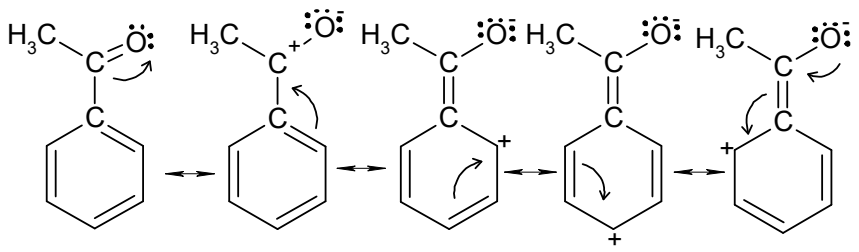
SAQ 2

How will you prepare 2,6-dihydroxyacetophenone from benzene-1,3-diol?

19.3 REACTIONS OF ARYL ALDEHYDES AND KETONES

The major differences between aromatic carbonyl compounds and most aliphatic analogues are that i) the carbonyl group of former reacts with nucleophile at a much slower rate ii) the aromatic ring of former also reacts with electrophile at a slower rate and iii) those reactions depending upon the presence of alpha hydrogen are not observed in the case of benzaldehyde.

The less reactivity of carbonyl group of aromatic aldehydes and ketones towards nucleophilic attack can be attributed to the resonance interaction between carbonyl group and aromatic ring.



Resonating structures of acetophenone

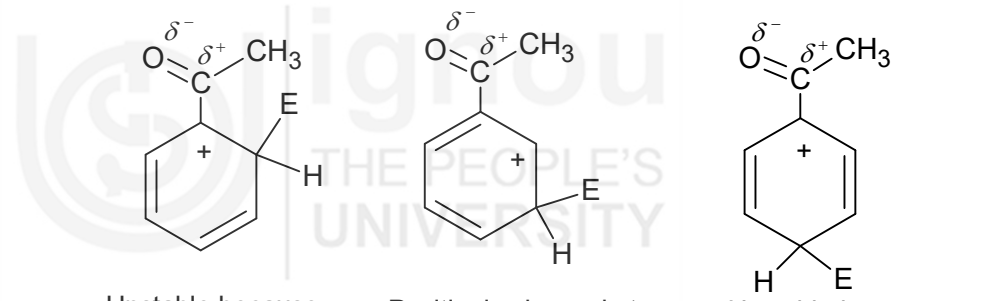
The result of this resonance interaction is

i) a weakening of the positive charge on the carbonyl carbon atom through dispersal of the charge into the ring, and

ii) deactivation of ring.

Because the carbon atom of carbonyl group attached to the ring is positively charged due to the electrongativity of oxygen atom, thus carbonyl group behaves as an electron withdrawing group and so it deactivates the ring towards electrophilic substitution reactions. As illustrated above, *ortho* and *para* positions have positive charges and the electron density at the *meta* position is not much affected by the carbonyl group. Therefore, the electrophiles preferably go to the *meta* position. Thus, both benzldehyde and acetophenone will form major *meta* disubstituted products and attack of electrophile will be slower than attack in benzene.

Formation of the major *meta* product can also be explained on the basis of the stability of the cyclohexadienyl cation intermediates formed on attack of electrophile. The intermediates for *ortho* and *para* substitution are particular unstable because each has a resonance structure in which there is a positive charge on the ring carbon that bears the electron-withdrawing substituent. Such situation is not observed in case of meta attack.



Unstable because of adjacent positively charged atoms

Positively charged atoms not adjacent, most stable intermrdiate

Unstable because of adjacent positively charged atoms

With the above general ideas, it will be easier to understand the reactions of aromatic aldehydes and ketones. Many of the reactions, which aliphatic aldehydes and ketones undergo, are also shown by aromatic aldehydes and ketones. In next sub-section, our focus mainly will be on the reactions, which show exceptional behaviors.

SAQ 3

Why are aromatic aldehydes and ketones less reactive than alphatic aldehydes and ketones for nucleophilic attack?

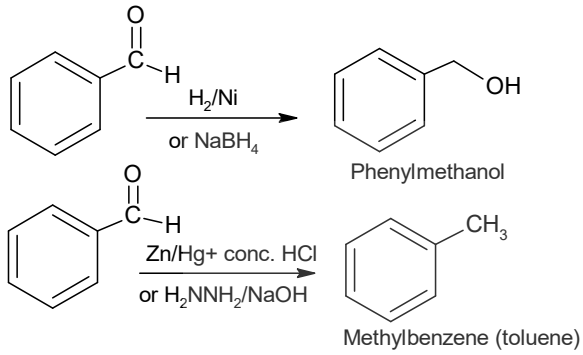
19.3.1 Benzaldehyde

Reactions of Aldehyde Group

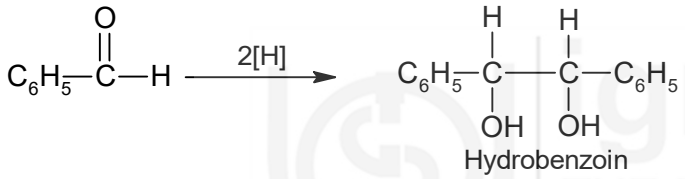
Even though the carbonyl group of benzaldehyde is less reactive than carbonyl group of aliphatic aldehydes, benzaldehyde gives many general reactions of aldehydes as described in previous unit. Benzaldehyde forms

many useful intermediate products with a range of nitrogen nucleophiles. Imines (Schiff bases) are formed with amines, hydrazones with hydrazines, semicarbazones from semicabazide and oximes from hyroxylamine. These products are of value in the synthesis of heterocycles.

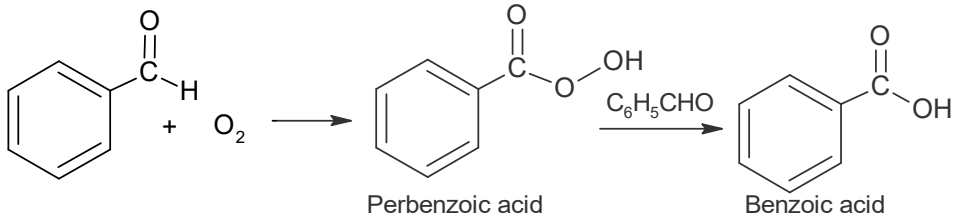
Catalytic hydrogenation and chemical reduction convert benzaldehyde to phenyl methanol (benzyl alcohol). On the other hand, Clemmension and Wolff-Kishnner reduction converts it into methylbenzene (toluene).



Benzaldehyde reacts with zinc and hydrochloric acid or with sodium amalgam and undergoes reductive dimerisation to give 1,2-diphenyl-1,2-ethanediol (hydrobenzoin):

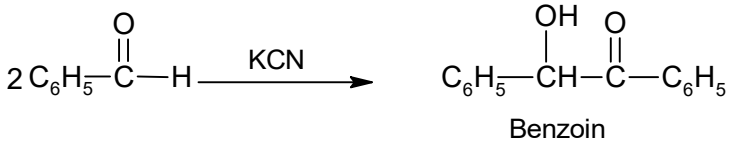


However, it does not reduce Fehling's solution but is easily oxidised by mild oxidising agents such as ammoniacal silver nitrate (Tollens' reagent). These two reactions are used to differentiate benzaldehyde from aliphatic aldehydes and ketones. Even atmospheric oxygen is enough to convert this to benzoic acid. When benzaldehyde is exposed to air, it forms a peroxide, perbenzoic acid, which oxidises another molecule of benzaldehyde as follows:

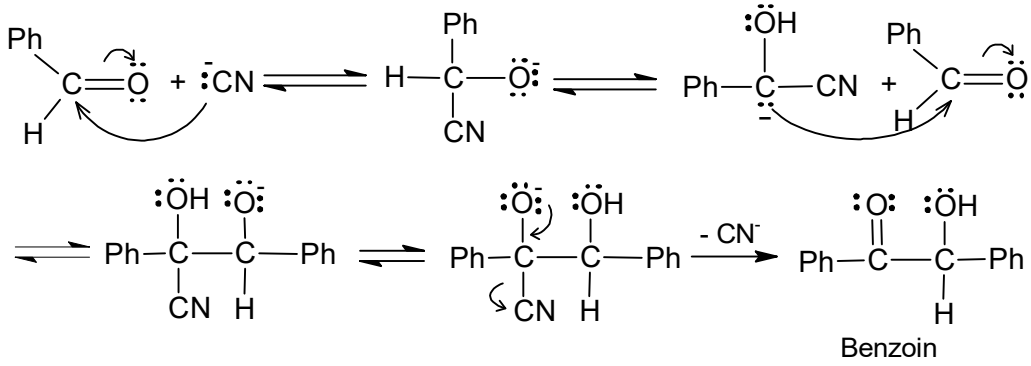


This type of oxidation, known as auto-oxidation, may be prevented by adding small amount of any antioxidant such as hydroquinone.

Formation of cyanohydrin from aromatic aldehydes and ketones with hydrogen cyanide is not a very useful reaction, but benzldehyde undergoes condensation reaction on refluxing with aqueous ethanolic potassium cyanide and forms benzoin. This condensation is known as **benzoin condensation**.



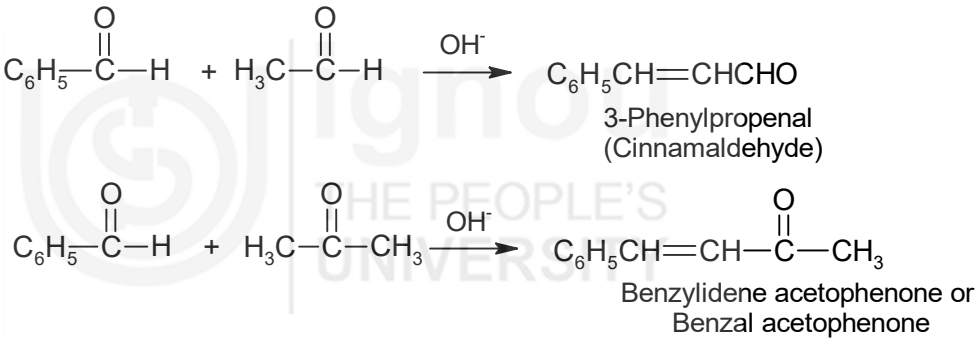
The mechanism of this condensation reaction is as follows:



Benzoin

As mentioned above, benzadehyde does not have an alpha hydrogen. Therefore, it cannot be enolised and therefore, enolate/carbanion cannot be generated from it. However, benzaldehyde can react with enlolates/carbanions generated from other aldehydes, ketones, esters, anhydrides, and so undergoes wide range of condensation reactions.

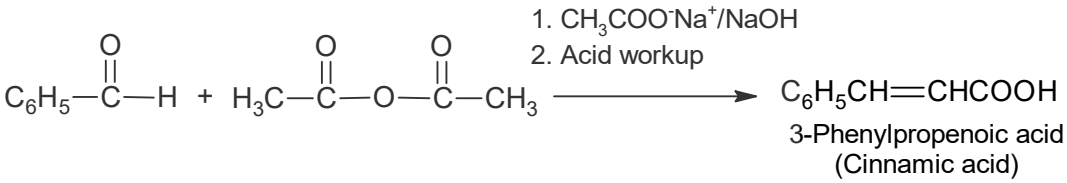
We have seen earlier that benzaldehyde undergoes mixed aldol condensation with aldehydes or ketones having α-hydrogen in the presence of alkali to form α, β-unsaturated carbonyl compounds. This reaction is also known as **Claisen-Schmidt reaction**.



3-Phenylpropenal
(Cinnamaldehyde)

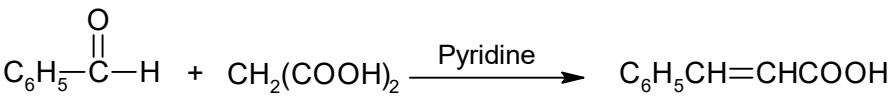
Benzylidene acetophenone or
Benzal acetophenone

On treatment with ethanoic anhydride and sodium ethanoate, benzaldehyde gives 3-phenylpropenoic acid (cinnamic acid). This condensation is known as **Perkin reaction**.



3-Phenylpropenoic acid
(Cinnamic acid)

Benzaldehyde also gives 3-phenylpropenoic acid with propanedioic acid (malonic acid) in the presence of pyridine. This reaction is known as **Knoevenagel condensation**.

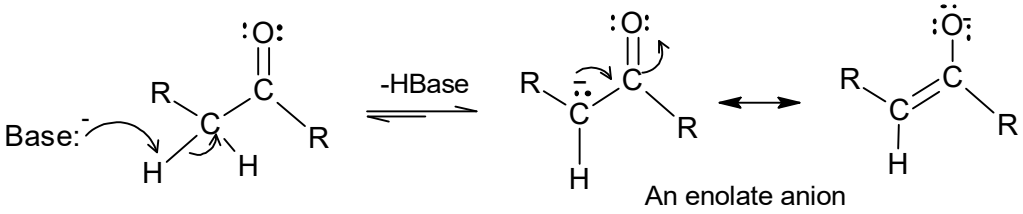


3-Phenylpropenoic acid
(cinnamic acid)

Mechanistically, both the named reactions discussed above proceed by a common pathway involving four steps:

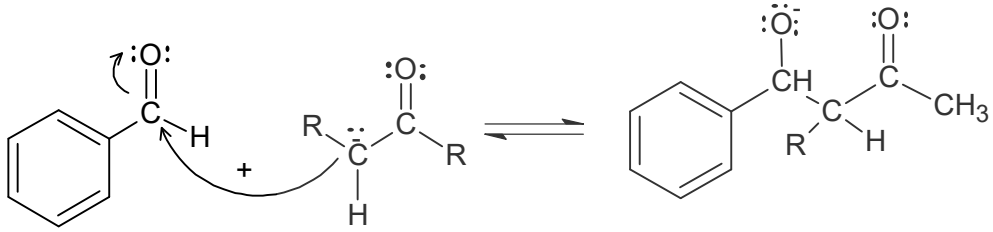
Step 1

Generation of a carbanion: Carbonyl compounds having active α-hydrogen generate the resonance-stabilised enolate anion on reaction with a base.



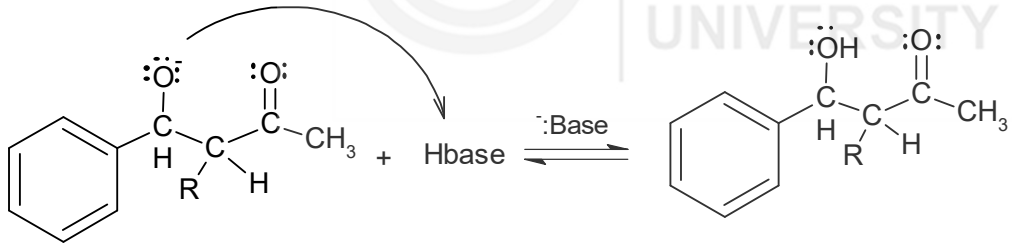
Step 2

Making a new C−C bond between a nucleophile and an electrophile: Nucleophilic addition of the enolate anion to the carbonyl carbon of benzaldehyde gives addition intermediate, oxyanion.



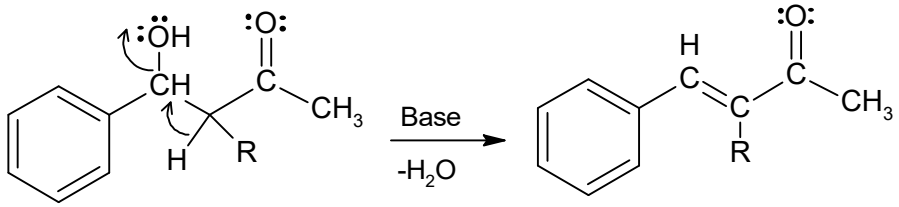
Step 3

Protonation of the oxyanion formed in the previous step: Reaction of the oxyanion intermediate with a proton donor gives the aldol product and generate a new base catalyst.

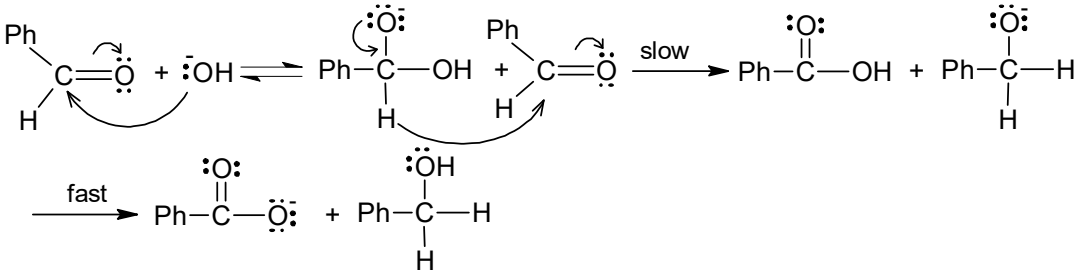


Step 4

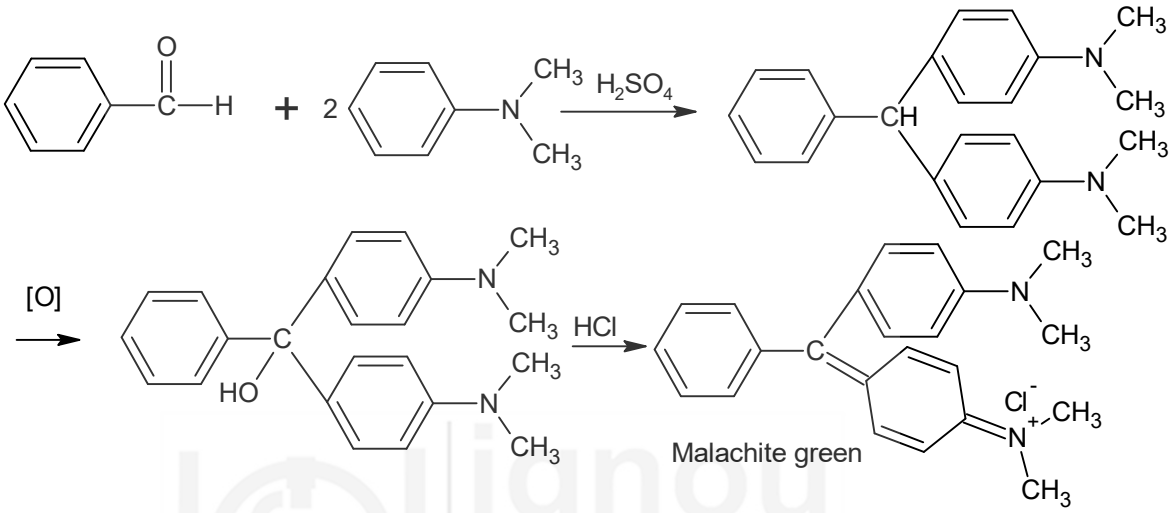
Dehydration of the aldol product: In such aldol condensation reactions, dehydration of the aldol product is rapid, which leads to formation of the more thermodynamically sable *α,β*-unsaturated product and prevent the retroaldol reaction from taking place.



Benzaldehyde undergoes Cannizzaro reaction as discussed with formaldehyde, in which two molecules of benzaldehyde react to produce one molecule of benzoic acid one molecule of benzyl alcohol as per scheme given below:



Condensation of benzaldehyde with phenols or tertiary aromatic amines in the presence of dehydrating agents, H_2SO_4 or $ZnCl_2$, gives triphenyl derivatives. Oxidation with lead dioxide followed by treatment with hydrochloric acid gives a dye, e.g.,



SAQ 4

How the following conversion can be carried out?

a) Benzoic acid from benzaldehyde

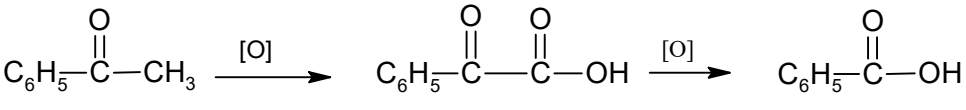
b) Benzyl alcohol from benzadehyde

c) toluene from benzaldehyde

19.3.2 Acetophenone

Acetophenone undergoes typical reactions of ketones, e.g., reduction with sodium and ethanol gives phenylethanol, Clemensen's reduction gives ethyl benzene. It undergoes addition reaction with hydrogen cyanide, hydroxylamine, etc. in the manner expected of a ketone, but because of low reactivity of the carbonyl group, acetophenone does not react with saturated aqueous sodium sulphate.

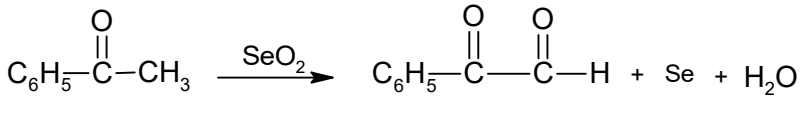
It is oxidised by cold potassium permanganate to give phenyl-2-oxoethanoic acid (phenyl glyoxolic) acid which gets further oxidised to benzoic acid:



Phenyl-2-oxoethanoic acid (Phenyl glyoxalic acid)

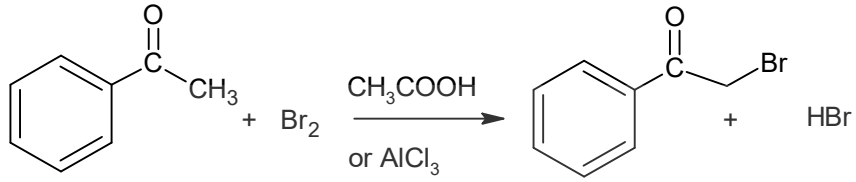
Benzoic acid

Oxidation with selenium dioxide gives phenyl-2-oxoethanal:



Phenyl-2-oxoethanal
(Phenyl glyoxal)

Acetophenone undergoes *α*-halogenation like aliphatic methyl ketones as illustrated by acid catalysed bromination of acetophenone.

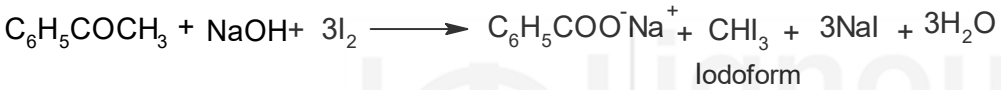


α–Bromoacetophenone
(2-bromo-1-phenylethanone)

On treatment with bromine in ether at 273 K in the presence of aluminium chloride, used as a catalyst, it also gives phenyl-1-bromo-2-ethanone (phenacyl bromide):

2-Chloro-1-phenylethanone is used as riot control agent (tear gas).

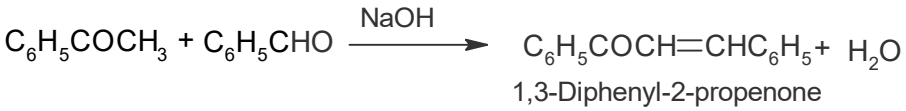
Acetophenone also undergoes iodoform reaction with iodine.



Iodoform

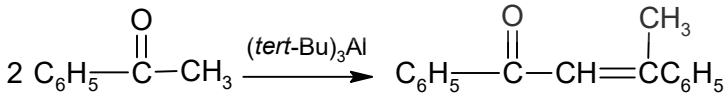
If we use one equivalent of aluminium chloride and bromine is added after the formation of aluminum chloride complex with acetophenone, nuclear bromination is taken place and major product will be 3'-bromoacetophenone.

The methyl group in acetophenone is adjacent to a carbonyl group. Therefore it can form stable carbanion/enolate and takes part as nucleophile in addition reaction and condensation reactions similar to aliphatic ketones.



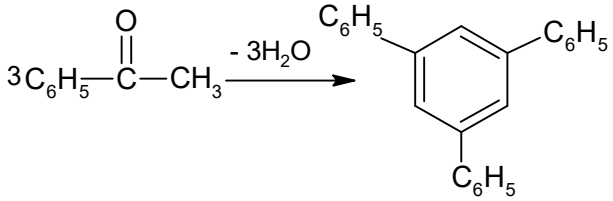
1,3-Diphenyl-2-propenone
(Chalcone)

Two molecules of acetophenone can also condense together in the presence of aluminium *tert* -butoxide to give 1,3 diphenyl-2-buten-1-one(dypnone):

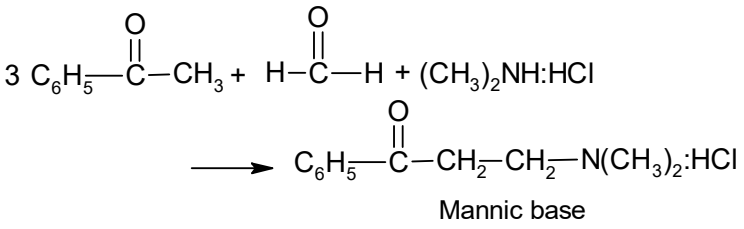


1,3-Diphenyl-2-buten-1-one
(Dypnone)

Condensation in the presence of hydrochloric acid forms 1,3,5-triphenylbenzene:



Acetophenone reacts with methanal (formaldehyde) and ammonia or a primary or secondary amine (as hydrochloride) to give ketoamines called Mannich bases. This reaction is called the **Mannich reaction**, e.g.,

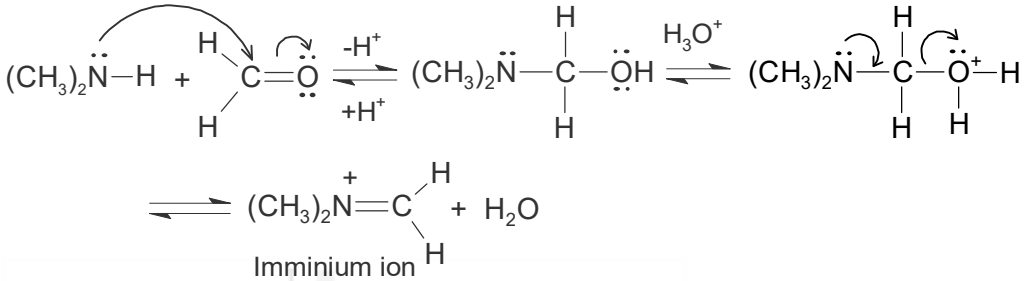


Mannic base

Mechanism of Mannich reaction:

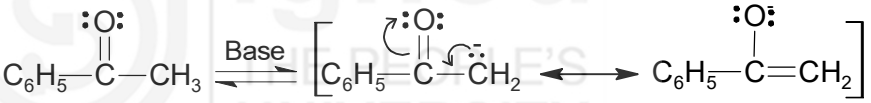
Three steps are involved in the Mannich reaction: Step 1: formation of Imminium ion, Step 2: formation of carbanion and Step 3: attack by carbanion.

Step 1: Formation of imminium ion

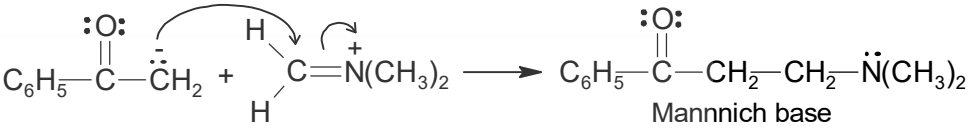


Imminium ion

Step 2: Formation of carbanion

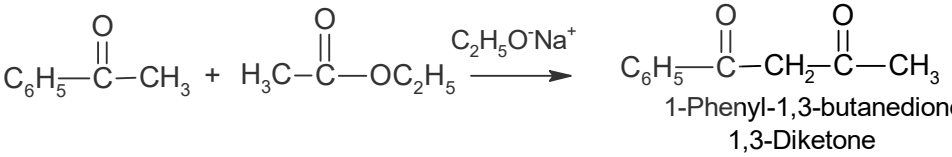


Step 3: Attack by carbanion



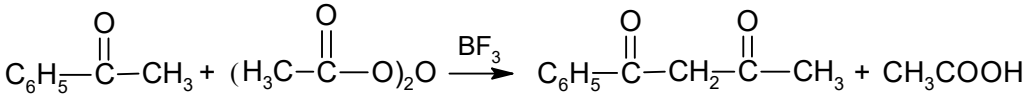
Mannnich base

1, 3-Diketones are formed from acetophenone by condensation either with ethyl ethanoate in the presence of sodium ethoxide or with ethanoic anhydride in the presence of boron trifluoride:



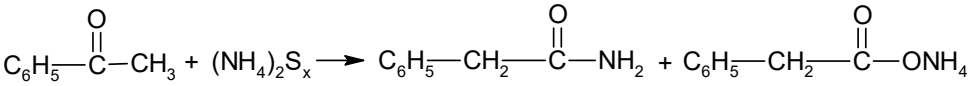
1-Phenyl-1,3-butanedione

1,3-Diketone



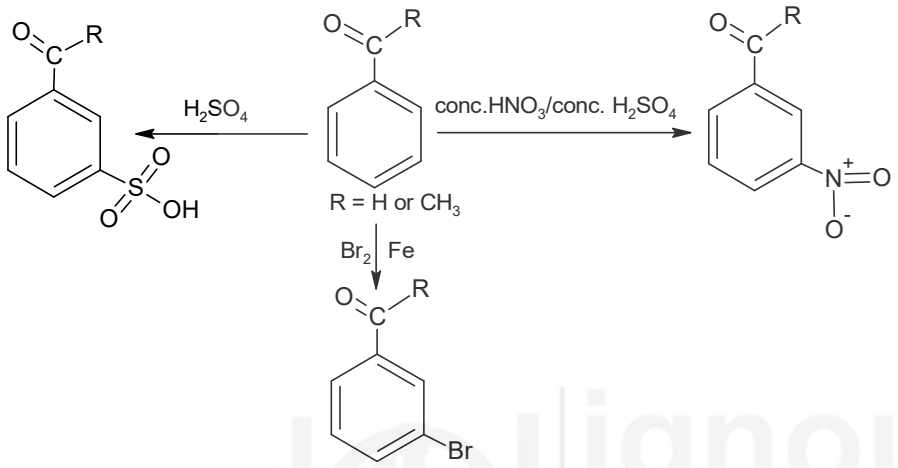
1,3-Diketone

By heating acetophenone with aqueous yellow ammonium polysuplhide, phenylethanamide and ammonium phenylethanoate are obtained (**Willgerodt reaction**):



19.3.3 Reactions due to the Benzene Ring

As we mentioned earlier, the carbonyl group is a deactivated in electrophilic aromatic substitution reactions and directs substitution to the *meta* positions. Therefore, benzaldeyde and phenylethanone are less reactive towards electrophilic substitution reactions than the benzene. Nitration and sulphonation are possible, but care must be taken to avoid interaction with the carbonyl group. Dilute nitric acid brings about oxidation of the –CHO group of benzaldehyde. Strong concentrated nitric and sulphuric acids are normally used in nitration reactions. As discussed above, ring halogenations depend on the reaction condition used. Both benzadehyde and acetophenone do not undergo Friedel-Craft reaction.



SAQ 5

Complete the following reactions:

a) $C_6H_5COCH_3 + C_6H_5CHO \xrightarrow{NaOH}$

b) $C_6H_5CHO + KCN$

c) $C_6H_5COCH_3 + CH_3COOC_2H_5 \xrightarrow{C_2H_5ONa}$

d) $C_6H_5COCH_3 + HCl \longrightarrow$

19.4 SUMMARY

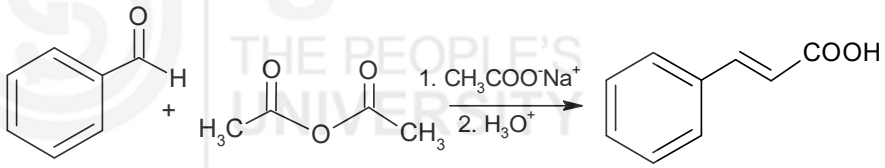
In this unit we have described the chemistry of aromatic aldeydes and ketones. We are summarising below what we have studied:

- Benzaldehyde can be prepared by the hydrolysis of (dichloromethyl) benzene and by the oxidation of toluene with chromium trioxide in acetic anhydride. It can also be prepared by direct formylation of benzene usimg several methos such as Gattermann-Koch reaction, Gattermann synthesis, Vilsmeier-Haack reaction, etc. Benzaldehyde can also be obtained from benzoic acid using Stephens reaction and from benzoyl chloride using Rosenmund reduction.
- Acetophenone can be prepared by the Friedel-Crafts acylation, Fries rearrangement and Hoesch reaction.

- Because of the resonance effect necleophilic reactions of the carbonyl group of benzaldehyde and acetophenone take place at a slower rate. Carbonyl group being an electron withdrawing group, it deactivate the benzene ring and the electrophile will preferably attack on *meta* positions of the ring.
- Benzaldehyde undergoes several types of condensation reactions and forms many useful synthetic intermediates, for example: Benzoin condensation, Claisen-Schmidt reaction, Perkin reaction, and Knoevenagel reaction.
- Acid catalysed bromination of acetophenone, brominates side chain. With methanal (formaldehyde) and ammonia or a primary or secondary amine (as hydrochloride), acetophenone undergoes Mannich reaction and forms Mannich base.

19.5 TERMINAL QUESTIONS

1. Write the steps involved in Sommelet reaction.
2. Draw resonating structures for the resonance-stabilised cation intermediates formed by attack of a nucleophile on *ortho, para* and *meta* position to carbonyl group of benzaldehyde.
3. Explain why is carbonyl group is meta directing?
4. Propose a reasonable mechanism for the following conversion.

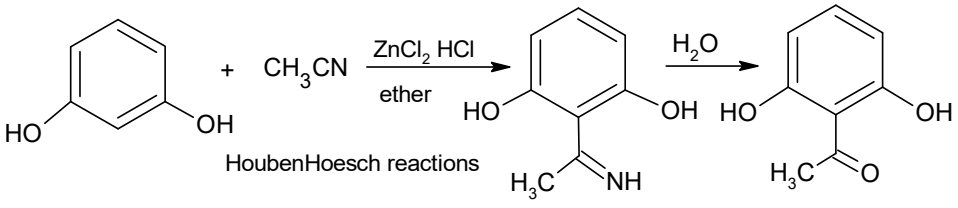


5. How will you bring about following conversions?
   a) Benzaldehyde to cinnamaldehyde
   b) Benzaldehyde to cinnamic acid
   c) Acetophenone to dypnone
   d) Acetophenone to 1,2,3-triphenylbenzene
   e) Acetophenone to 1-Phenyl-1,3-butanedione

19.6 ANSWERS

Self-Assessment Questions

1. c)
2.



3. A weakening of the positive charge on the carbonyl carbon atom through dispersal of the charge into the ring through resonance effect is mainly responsible for the lesser reactivity of aromatic aldehydes and ketones than alphatic aldehydes and ketones for nucleophilic attack.

4. a) By oxidation methods. Benzaldehyde can easily be converted to acid even with mild oxidizing agents.

   b) By the catalytical hydrogenation or chemical reduction using Lithium aluminium hydride or sodium borohydride.

   c) By Clemmension reduction or Wolff-Kishner reduction method.

5. a) $C_6H_5COCH_3 + C_6H_5CHO \longrightarrow C_6H_5COCH_2{=}CHC_6H_5$

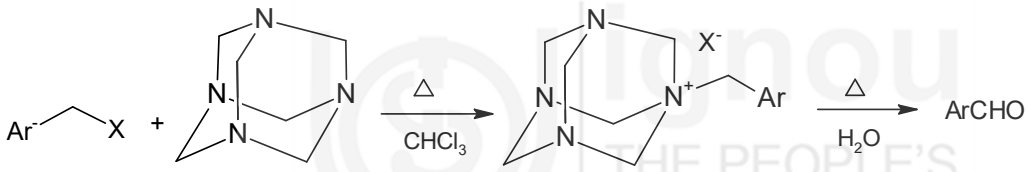
   b) $C_6H_5CHO + KCN \longrightarrow C_6H_5\underset{\displaystyle OH}{\underset{|}{C}}HCOC_6H_5$

   c) $C_6H_5COCH_3 + CH_3COOC_2H_5 \xrightarrow{C_2H_5ONa} C_6H_5COCH_2COCH_3$

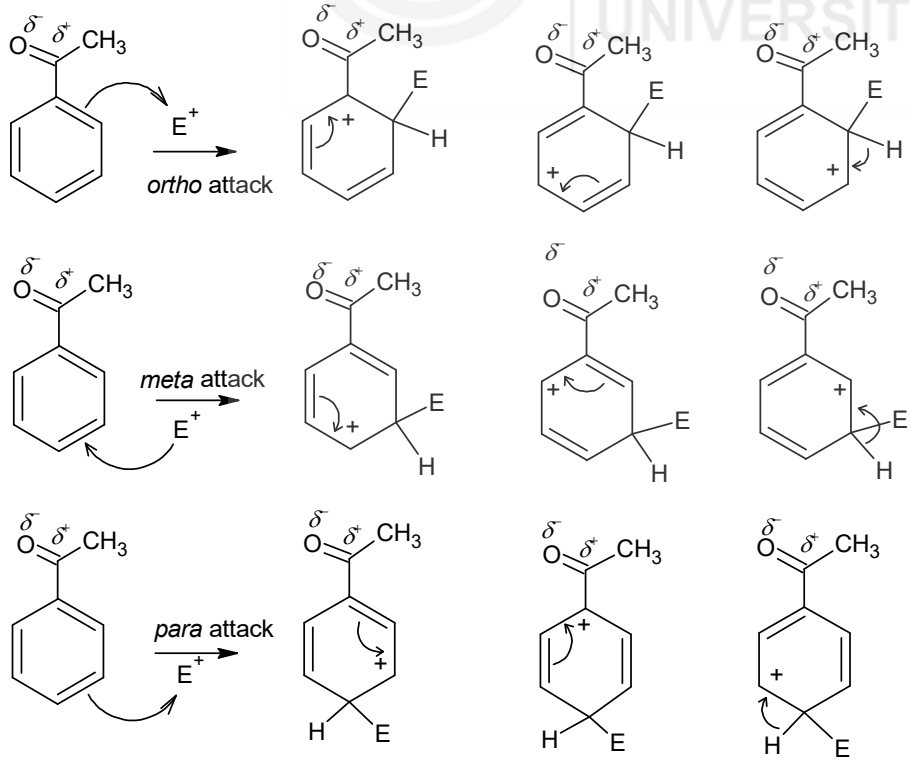
   d) $C_6H_5COCH_3 + HCl \longrightarrow$ 1,3,5-triphenylbenzene

Terminal Questions

1.



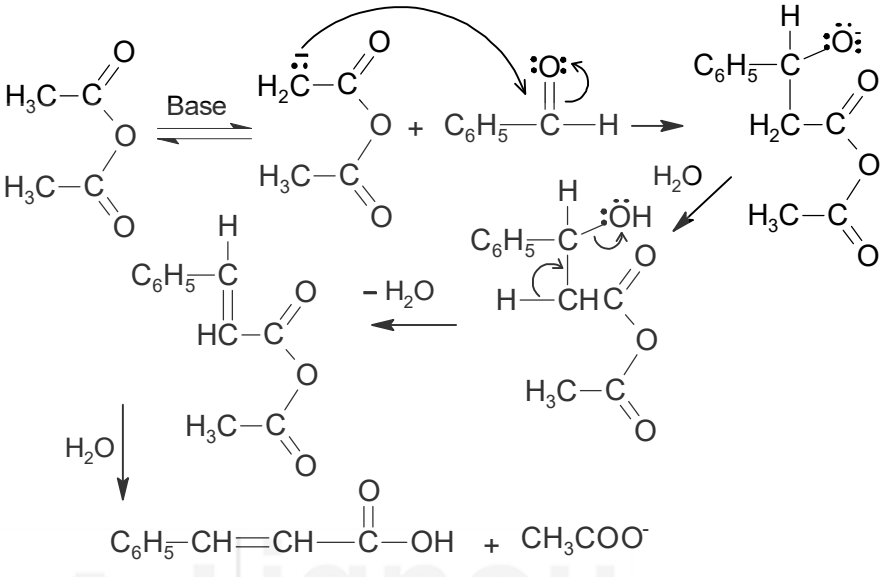
2.



3. The resonace structures drawn for the intermediates formed on ortho , para and meta attack of electophile, clearly indicate that the intermediates for ortho and para substitutions are particular unstable

because each has a resonance structure in which there is a positive charge on the carbon that bears the electron-withdrawing substituent. Such situation is not observed in case of meta attack.

4. Five steps are involved in this reaction: Step 1: Formation of carbanion Step 2: Attack by carbanion on the aromatic carbonyl compound to form alkoxide, Step 3: protonation of the alkoxide ion to form an aldol type compound. Step 4: dehydration, the hydroxyl group and neighbouring hydrogen are removed as water and Step 5: hydration



5. a) $C_6H_5CHO + CH_3CHO \xrightarrow{OH^-} C_6H_5CH{=}CHCHO$

3-Phenylpropenal
(cinnamaldehyde)

b) $C_6H_5CHO + (CH_3CO)_2O \longrightarrow C_6H_5CH{=}CHCOOH$

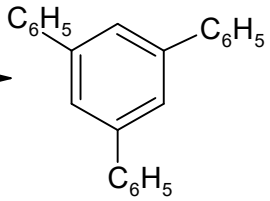
3-Phenylpropenoic acid
(cinnamic acid)

$C_6H_5CHO + CH_2(COOH)_2 \xrightarrow{\text{Pyridine}} C_6H_5CH{=}CHCOOH$

3-Phenylpropenoic acid
(cinnamic acid)

c) $2\ C_6H_5COCH_3 \xrightarrow{(tert\text{-}Bu)_3Al} C_6H_5COCH{=}CC_6H_5$

Dypnone

d) $3\ C_6H_5COCH_3 \xrightarrow{-3H_2O}$ 

e) $C_6H_5COCH_3 + H_3CCOOC_2H_5 \xrightarrow{C_2H_5O^-Na^+} C_6H_5COCH_2COCH_3$

1-Phenyl-1,3-butanedione
1,3-Diketone

FURTHER READING

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